American Petroleum Institute

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Re: Docket No. EPA–HQ–ORD–2013–0292

The American Petroleum Institute (API)[1] respectfully submits the following supplemental comments in response to the U.S. Environmental Protection Agency's (EPA or Agency) request for comments on the draft Cumulative Risk Assessment (CRA) Guidelines for Planning and Problem Formulation. API and API member companies are committed to working with regulatory agencies and stakeholders to foster solutions that ensure responsible and sustainable practices within the complex environments where we operate.

EPA has been engaged in a long-term effort to confront the potential risks posed by simultaneous exposure to both chemical and non-chemical stressors. The groundwork for cumulative risk assessment (CRA) and its potential contribution to environmental justice (EJ) initiatives was initially conceived as far back as 1997, as detailed in Appendix A of the draft guidelines. Over time, the EPA and various external bodies have issued strategic directives to advance cumulative risk assessment practices (*e.g.*, EPA, 2003; 2014; NRC, 2009; NEJAC, 2004). The current draft guidance document titled *"Guidelines for Cumulative Risk Assessment: Planning and Problem Formulation"* (EPA, 2023a) is the agency's latest attempt to advance the implementation of CRA. This document aims to clarify the aspects of planning, scoping, and problem formulation concerning CRAs.

CRAs may offer comprehensive perspectives on the influence of multiple stressors, the issues' complexity challenges the development of methodologies. While API commends the agency's effort to establish a structured framework for conducting CRAs, there are certain areas that require attention before the widespread adoption of CRA methodologies.

- *EPA can improve the document by providing specific implementation directives and concrete examples and exploring quantitative or qualitative methodologies to underpin the analysis of non-chemical stressors.* It is challenging to ascertain the circumstances necessitating the initiation of a CRA and the appropriate methods. For example, while the document underscores the utilization of CRA to address potential environmental justice concerns, the exact initiating factors, and triggers for incorporating CRA into an environmental justice assessment require further clarification.
- *The EPA must recognize that a significant constraint in conducting CRAs is the fact that many of the objectives surpass the capabilities of existing methodologies and tools.* It appears premature to present detailed planning and problem formulation steps without

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concurrently presenting the tools or means for guiding decisions on initiating and carrying out a CRA or establishing quantifiable connections between stressors and adverse health effects.

- *EPA needs to highlight the difference between a cumulative impacts assessment (CIA) and a cumulative risk assessment (CRA), particularly regarding scope and applicability to non-chemical stressors, to avoid confusion.* EPA's Office of Research and Development (ORD) and Office of Pollution Prevention and Toxics (OPPT) under the Toxic Substances Control Act (TSCA) have issued multiple cumulative assessment guidance documents. Notably, EPA released the "Cumulative Impacts Research: Recommendations for EPA's Office of Research and Development (Final Report)," which, much like the current draft CRA guidelines, outlined foundational concepts and proposed overarching strategies for conducting CIAs.
- *Establishing alignment within the EPA and other federal agencies engaged in this work is pivotal to harmonizing methodologies, optimizing resource allocation (including study design), and enhancing the acceptability of these approaches.* For example, under TSCA, OPPT introduced general CRA guidelines (EPA, 2023b) and published a proposal for a phthalate CRA (EPA, 2023c). Notably, the OPPT CRA guidelines explicitly indicate that CRA is *not* designed to address cumulative impacts from non-chemical stressors. Given that the ORD and OPPT guidance documents operate in conjunction to fulfill regulatory requirements under TSCA, it becomes crucial for their CRA approaches to be harmonized - this involves clearly explaining the differences between these assessment types and their regulatory integration.

Below, we provide more detailed comments on key areas of concern in EPA's draft CRA guidelines.

Detailed Comments

1. ***Clarification of Initiating Factors:*** Section 2 of the draft CRA guidelines introduces the concept of "initiating factors," which trigger the need for a CRA. However, the extent to which these factors inform the necessity of conducting a CRA remains unclear.

    - The initiating factors reflect a broad range of circumstances – for example, complying with national regulations (*e.g*., compliance with the Food Quality Protection Act [FQPA]), facility permitting, and addressing specific community concerns regarding exposure or health status. With such a diverse range of applications and stakeholders, it becomes crucial for the EPA to provide specific and structured guidance on (1) initiating an assessment, (2) documenting the initiation, and (3) conducting the assessment so that its overall objective is clear, and the results have appropriate context.
    - The guidelines need to incorporate specific initiating criteria or thresholds that stakeholders and risk assessors need to consider as part of determining if a CRA is required. To support this process, the guidelines could include a decision tree highlighting each step and the pertinent questions that need to be asked to consider each initiating factor. Moreover, specific triggers that may warrant moving forward with an assessment should be identified. While the draft CRA guidelines currently list several initiating factors on pages 7 and 8; it would be useful to provide examples of how each

factor could be assessed, coupled with criteria guiding the decision for inclusion or exclusion.
- Guidelines should be established to facilitate effective communication of the results obtained during the evaluation of initiating factors. This transparent communication mechanism is vital to ensuring that all stakeholders can contribute their insights and feedback based on the rationale underlying the decision to conduct or not conduct a CRA.

2. ***The draft CRA guidelines notably lack specific examples of CRAs addressing non-chemical stressors.*** This absence indicates a gap in available methodologies for assessing risks from such stressors. The examples and resources presented in the main text boxes and Appendix A predominantly pertain to traditional chemical-only risk assessments.

   - Appendix A references several publications and EPA-hosted public webinars that explore CRA methodologies encompassing multiple stressors, including non-chemical stressors, effect modifiers, decision frameworks, and challenges tied to integrating qualitative factors into risk assessments. It is essential to understand how the insights from these sources influenced the formulation of the proposed guidelines. Can the CRA guidelines incorporate an explanation of what was gleaned from these resources?
   - In Appendix A (Section A.2), chemical-only mixture CRA examples are provided. However, risk assessors seek examples that encompass non-chemical stressors. Potentially, the Risk Assessment Guidance for Superfund (RAGS) could be considered as it already covers cumulative risk assessments involving multiple pathways and chemicals, leaving room for the inclusion of non-chemical stressors.
   - Incorporating a hypothetical CRA example that integrates non-chemical stressors could be highly instructive. Placing this example in Section A.3 ("Looking Ahead") of Appendix A or within the main text would be fitting. Or at the very least, the main text should reference this hypothetical example in Appendix A.
   - Similarly, the text box examples within the main text should account for non-chemical stressors. For instance, Text Box 2 outlines the purpose of a CRA, yet the example provided exclusively incorporates chemical stressors from two facilities. EPA could clarify by providing information on how non-chemical stressors could be incorporated in the example scenario.
   - Many risk assessors are proficient in evaluating cumulative risks stemming from multiple chemical sources across various environmental media (air, water, sediment, surface water, and soil), and even encompassing secondary pathways when necessary. Thus, the examples included in the bulleted list in Section 3.6 ("Adverse Effect and Exposure Stressor Groups"), could extend to include discussions on non-chemical stressors.

   The lack of sound examples of CRAs, even hypothetical ones, in the draft guidelines raises questions about the availability of applicable tools for conducting CRAs. The methods/tools mentioned in the guidelines do not appear particularly tailored for CRAs, with references to chemical stressor-specific instances like dose and response relationships, practices that are well-established and have limited applicability, and/or are already covered by RAGS. If there are applicable tools for CRAs, especially in relation to non-chemical stressors and exposure modifiers, descriptions of these tools and their potential application, even in hypothetical scenarios, should be presented. In the absence of tools to address these aspects of CRAs, the

issuance of CRA guidelines might be considered premature. However, should tools emerge for incorporating non-chemical stressors in CRAs, it's crucial that these tools be well-developed and validated, rather than being deployed in the early developmental stages.

3. ***Refinement of Conceptual Model Development:*** Guidance on creating a conceptual model (CM) for CRAs requires improvement. Although the guidance touches on CM development, it can be enhanced to better support risk assessors through constructing a coherent and practical CM that effectively incorporates both chemical and non-chemical stressors.

   - The draft CRA guidelines underscore the need for a conceptual model (CM) encompassing both chemical and non-chemical stressors. However, the guidance lacks clear instructions on how to construct such a CM. While an example CM is provided in Appendix C, it appears as a complex web of potential connections between various stressors - creating more confusion. The example itself is repetitive and alludes to the same indicators in different areas. The multitude of proposed (and overlapping) stressor relationships linked to cardiovascular disease (CVD) highlights the intricacy of CRAs. However, the guidance document does not describe how this CM was developed.
   - A more explicit CM example is necessary, one that systematically guides risk assessors through each phase of CM development. Utilizing decision trees, the CM development process could map how the assessment was initiated (referring to key initiating criteria, as mentioned in Comment 1 above), how these criteria guide CM decisions, and then how factors (chemical and non-chemical stressors) are chosen for inclusion (or exclusion) in the final CM. An example CM could provide guidelines and specific criteria for CM development, rather than merely depicting a finished product.
   - The final CM could visibly portray connections between stressors, indicating which relationships can be quantitatively evaluated and which require qualitative consideration. It should highlight areas where uncertainty within the CRA is more pronounced. Introducing several interconnected CMs could clarify potential stressor connections. Careful attention must be paid to confounding factors and potential correlations arising from the multifaceted evaluations.
   - The example CM should spotlight the key initiating factors and objectives (potentially centered on quantitative factors like chemical risks), onto which non-quantifiable elements can be superimposed as potential modifiers or supplementary stressors. However, these non-quantifiable factors should only be illustrated as potentially impacting the overall assessment outcome (potentially shaded differently or indicated with dashed lines). They can be described as introducing potential uncertainty into the CRA. If a comprehensive evaluation of non-chemical stressors is intended, this should also be evident in the CM. In that case, the guidelines should discuss the suitable tools for conducting these evaluations. If quantifying non-chemical stressors for CRAs is unfeasible, existing methods like those found in chemical risk assessments (e.g., RAGS-style) could be considered for addressing non-chemical stressors within the uncertainty discourse, rather than enforcing an exhaustive CRA.
   - As discussed further in Comment 6, Chapter 3 (“Problem Formulation”) is divided into Sections 3.1-3.10. Many of these sections would be better positioned as subsections under Section 3.2 (“Conceptual Model”). Given that the CM is a central product of this phase of CRA design, incorporating subsections like 3.3 (“Consideration of Stressors”),

3.4 (“Receptors of Potential Interest”), 3.5 (“Exposure-Response Modifiers”), and 3.6 (“Adverse Effect and Exposure Stressor Groups”) into the CM section would provide clarity on CM development components.

- The mention of a “secondary CM” in Section 2 (“Planning and Scoping”), necessary for different risk management interventions, seems odd when introduced prior to discussing the development of the primary CM. It might be more fitting to address the secondary CM within the CM discussion in Section 3, as another CM feeding into the primary CM.
- Careful consideration on multiple CMs so that confounders and improper correlations are not made from the excess of factors being used

4. ***Evaluation of Non-Chemical Stressors:*** A distinct and comprehensive discussion on how non-chemical stressors will be evaluated within CRAs is missing. Detailed guidance and examples are necessary to address the complex process of evaluating non-chemical stressors, whether through quantitative or qualitative means.

   - While Table 1 outlines key factors applicable to non-chemical stressors, it offers minimal guidance on their use and assessment. The draft guidelines lack specific instructions or hypothetical examples of conducting evaluations of non-chemical stressors. Although Appendix D provides a broad discussion on this topic, including suggested CRA frameworks and a decision tree example would be helpful. Questions to be addressed include: Will non-chemical stressors undergo quantitative or qualitative evaluations? What tools are available for these evaluations?
   - The CRA guidance should discuss *how* non-chemical stressors should be assessed in the CRA (*i.e.*, qualitatively or quantitatively, the rationale for either approach, the tools that can be applied to their evaluation, and example evaluations). EPA’s Integrated Risk Information System (IRIS) comes to mind when considering the integration of qualitative information in quantitative assessments. IRIS provides the methodology for quantifying chemical risks (*i.e.*, developing toxicity reference values). Will EPA consider developing what will be the equivalent of toxicity reference values for non-chemical stressors? Or will the approach to evaluating these stressors be qualitative?
   - Section 3 of the draft guidelines briefly discusses how epidemiology studies might be a data source for CRAs, stating epidemiology studies “link nonchemical stressors to population vulnerabilities in many contexts.” While the draft guidelines acknowledge the potential limitations in epidemiology studies, API also recognizes that epidemiology studies have inherent limitations related to potential biases, confounding variables and effect modifiers that are not always adequately adjusted for. API recommends that the EPA outlines considerations for epidemiology studies, including but not limited to appropriate types of study designs that are best suited to provide robust quantitative estimates of dose-response relationships, what relevant characteristics of underlying population to consider, generalizability, interactions/joint effects, etc. Such studies might encompass chemical and non-chemical stressors and evaluate how possible relationships among stressors could affect human health and ecological outcomes. (EPA, 2023a, p. 24). Utilizing the study titled "A Matrix for Bridging the Epidemiology and Risk Assessment Gap" could aid in providing context. This study helps to contextualize the gaps that frequently emerge between the data requirements of risk assessment and the findings from epidemiology studies.

- The potential confounding variables are often the non-chemical stressors that a CRA would aim to evaluate (*i.e.*, often related to socioeconomic factors, such as education and diet; medical conditions; and immutable factors, such as genetics, age, and sex). API asks the agency to clarify how epidemiology studies would be used in a CRA to evaluate risks associated with non-chemical stressors.
- The distinction between non-chemical stressors and exposure-response modifiers is unclear. As noted in Text Box 6, these two risk considerations "overlap," and it is possible for "a factor to be both an exposure-response modifier and a stressor" (EPA, 2023a, p. 25). The supporting discussion seems to distinguish between "vulnerability factors," which act as exposure-response modifiers, *versus* factors with a clear toxicological or exposure connection, which is evaluated as stressors (EPA, 2023a). However, this clarity becomes clouded by the last bullet in Section 3.6, which introduces vulnerability within the context of stressors. Without explicit criteria to ascertain whether a vulnerability factor should be deemed an exposure-response modifier or a stressor, it might be simpler to classify vulnerability factors solely as exposure-response modifiers. This adjustment would likely prove more practical, particularly given the intricacies of establishing dose-response relationships for "vulnerability factors." Integrating such factors into complex chemical risk assessments could be challenging.
- EPA's approach to identifying both chemical and non-chemical stressors appear overly generic, encompassing an extensive list of potential stressors. The guidance lacks clear instructions on how stressors should be chosen and subsequently evaluated. While the agency acknowledges flexibility of stressor selection as a feature CRA, the absence of more structured guidance risks turning stressor selection as inconsistent among different assessors.
- If the responsibility for evaluating these non-chemical stressors falls within the jurisdiction of the EPA, it becomes essential to determine how the evaluation would be conducted when exposures are transient (e.g., releasees), whether they are current or historical. The challenge arises when attempting to strike a balance – introducing too many factors could potentially confound results, leading to a situation where no specific site stands out as a distinct "priority." In essence, the inclusion of numerous factors might inadvertently result in a scenario where all sites appear to hold equal significance.

The lack of novel quantitative or qualitative approaches to address the incorporation of non-chemical stressors into CRAs undercuts the planning and scoping of CRAs. What would be the purpose of identifying initiating factors without understanding how, or if, those factors can be evaluated to inform decision-making? This issue comes to the forefront in Section 3.8 ("Analysis Plan"). In this Section, EPA describes several key steps when planning an analysis. One of the steps in this process is "Identification and Selection of CRA Techniques/Methods to Apply to Integrated Stressor Groups," which are further described as risk assessment methods and procedures that might be used to conduct a CRA. The draft guidelines then point the reader to traditional risk assessment resources, including the RAGS. These resources need to be improved to address the complex cumulative risk scenarios theoretically proposed in scoping steps (*i.e.*, those inclusive of non-chemical stressors). RAGS relies upon IRIS toxicity reference values (which include relevant modifiers in the uncertainty factor selection); this should be noted so that the multi-pathway, multi-chemical,

multi-media RAGS approach does not get overlooked when the key exposures in a CM are chemical stressors.

5. ***Addressing Uncertainty:*** A crucial aspect of any risk assessment, the treatment of uncertainty, warrants clearer guidance within the draft CRA document. Elaborating on strategies to handle uncertainty in CRAs would enhance the document's utility and the reliability of its outcomes.

    - The draft guidelines state that "[e]arly consideration also must be given to the approach, methods, and metrics that will be used to evaluate variability and uncertainty. These approaches might be quantitative or qualitative, and they address data evaluation, procedures, measures, methods, and models used in the CRA" (EPA, 2023a, p. 31). However, there needs to be further discussion on how these assessments can address uncertainty quantitatively. Some discussion related to CRA of pesticides, with an example of one uncertainty factor (UF) being applied to a group of chemicals, rather than UFs for each of the chemicals, is provided in Appendix B of the draft guidelines. The guidelines note that this approach reduces "the potential for a poorly studied chemical (with a very large uncertainty factor) to drive the calculation of the mixture risk" (EPA, 2023a, p. B-13). This approach seems reasonable for a chemical mixture, so long as care to avoid duplicative "uncertainty factors" beyond those already used to develop toxicity reference doses (such as in IRIS assessments). An example of how UFs might be applied for non-chemical stressors or groups of non-chemical stressors would be helpful. The uncertainty would also be evaluated qualitatively if a non-chemical stressor is evaluated qualitatively.
    - Suppose the use of quantitative UFs is being considered for CRAs. In that case, there needs to be agreement on how to implement these UFs, evaluating how they would overlap with the UFs currently used in chemical risk assessment. For example, there is a UF of 10 for variation in susceptibility among the population (*i.e.*, inter-individual variability) intended to address chemical-specific uncertainty in toxicokinetics and toxicodynamics. Some factors can be applied to address database deficiencies. However, there is likely some overlap between chemical specific UFs and vulnerability based on non-chemical stressors, which should be considered. For example, certain genetic differences in the metabolism of a chemical would be accounted for in the UF of 10. Still, those metabolic differences could also be caused by or modified by other environmental non-chemical stressors, such as diet, exercise, *etc.* (which could be associated with socioeconomic factors). The CRA guidelines need to describe that distinction.
    - To the extent that quantitative approaches can be used, these approaches need to be used to characterize uncertainty rather than account for uncertainty. It would not be advisable to apply UFs to account for uncertainty in CIAs, mainly since the uncertainty is likely to be profound. A quantitative uncertainty analysis/discussion is the preferred pathway whenever possible; however, given the breadth of issues that could be potentially addressed in a CIA, a qualitative uncertainty discussion seems most appropriate for a CRA that will include the evaluation of non-chemical stressors. The guidelines note that a CRA is feasible in several places when there is an "acceptable level of uncertainty" (*e.g.*, EPA, 2023a, p. 4). However, there is no guidance on how an acceptable level of uncertainty is defined. This is a critical factor that EPA needs to address; there is

uncertainty in all the stressor measurements, and if there are no bounds on acceptable uncertainty, the assessment will be limited to its applicability to address and prioritize specific risk concerns.

- Also, worth considering is whether the proposed guidance essentially amounts to a modification of the IRIS reference dose derivation protocols, making a separate CRA document unnecessary. If the primary requirement is enhanced transparency in the selection of "safety factors" within IRIS or other EPA program assessments, it might be more prudent to address this within those respective programs. Mandating an entirely new qualitative assessment process, where assessors start each assessment from scratch with a fresh literature search, might not be the most efficient approach.

As discussed above, we recommend illustrating potential sources of uncertainty in the CM upfront, during the problem planning and formulation stages, adjusting the CM iteratively as the assessment progresses, and then providing a qualitative narrative discussion of how the evaluation would deal with these uncertainties in its conclusions, and how these uncertainties should be considered for guiding risk management decisions.

6. ***Enhanced Organization and Clarity:*** Several readers have highlighted the need for better organization and clarity within the document. Streamlining content, improving the logical flow, and ensuring consistency in terminology would enhance the overall accessibility and utility of the guidelines.

   - There is a significant overlap between the two main chapters of the draft CRA guidance document (*i.e.*, Chapter 2, "Cumulative Risk Assessment Planning and Scoping," and Chapter 3, "Problem Formulation"). It may be better to focus Chapter 2 on steps that should be followed to determine whether a CRA is needed. That chapter could be titled "Cumulative Risk Assessment Initiation and Scoping." Within the chapter, clear guidelines and criteria would be provided to help stakeholders determine whether a CRA is needed and how to document the basis of that need (*i.e.*, what is the overall objective of the CRA?). Chapter 3 could then be titled "Planning and Problem Formulation," laying out the next steps after determining that a CRA is needed. This chapter would provide guidance on developing a CM that considers chemical and non-chemical stressors and should provide clear guidelines on how each stressor will fit into the CM. For both chapters, decision trees for each step of the CRA development (from initiation through CM finalization) should be presented to guide risk assessors/managers.
   - The current "Problem Formulation" chapter (Chapter 3) is divided into Sections 3.1-3.10. However, many of these sections should instead be subsections of the CM section (Section 3.2). The CM is one of the main outputs of this phase of designing a CRA, so it makes sense that a large part of the problem formulation process would be devoted to its development. Sections 3.3 ("Consideration of Stressors"), 3.4 ("Receptors of Potential Interest"), 3.5 ("Exposure-Response Modifiers"), and 3.6 ("Adverse Effect and Exposure Stressor Groups") all address parts of CM development, so we would recommend organizing these as subsections within the CM section so that it is clear what is involved in CM development.
   - Sections 3.7 ("Integration of Data for Examining Stressor-Response Relationship(s)") and 3.8 ("Analysis Plan") also seem to be related in that they both involve using the CM to

integrate the key information and approaches to develop the overall Analysis Plan. The two could be grouped into one section.

- Section 3.9 (Uncertainty and Variability) seems to stand alone. Still, it would be helpful to suggest that the risk assessor highlight sections of the CM that are more or less uncertain so that the uncertainty in the assessment can be clearly illustrated. This could be an addition to the CM that happens towards the end of the problem formulation step. It would also be helpful to compare/contrast how the Uncertainty Assessment portions of RAGS can be adapted to include qualitative discussion of non-chemical stressors to enable RAGS multi-pathway, multi-chemical, multi-media "cumulative" assessments to include these without compelling a new standalone CRA that would have no quantitative bearing on risk management decisions for lack of quantitative tools to incorporate the non-chemical stressor.
- Section 3.10 is called "Next Steps," but it may be better to break this section out into "Independent Peer Review of the CRA," "Risk Characterization," and "Risk Communication."

7. ***Consistency with Existing Programs:*** EPA has released other cumulative impact/risk assessment strategies and approaches under other programs (e.g., TSCA, Clean Air Act [CAA]). This guidance document should address how those recently released approaches are consistent (or not) with the principles outlined in the CRA guidelines.

    - In February 2023, EPA's OPPT published "Draft Proposed Principles of Cumulative Risk Assessment under the Toxic Substances Control Act" (EPA, 2023b). Overall, these guidelines are also vague and lack clear descriptions of how the proposed principles would be implemented, and how CRA can be used to quantify risk and guide risk management decisions. There are some apparent differences between OPPT's draft guidelines for CRA under TSCA and the draft CRA guidelines that are the subject of these comments (*i.e.*, issued by EPA's ORD). One key difference is that OPPT's proposed principles for CRA under TSCA specifically state that "this draft CRA principles document does not address cumulative impacts, which refer to the total burden—positive, neutral, or negative—from chemical and non-chemical stressors and their interactions that affect the health, well-being, and quality of life of an individual, community, or population at a given point in time or over a period of time" (EPA, 2023b, p. 6). They also note that "toxicological similarity" and "evidence of co-exposure over a relevant timeframe… will be the principal considerations determining a cumulative chemical group for CRA under TSCA" (EPA, 2023b, p. 9). The OPPT principles of CRA under TSCA focus only on chemical evaluation, considering chemical mixtures (*e.g.*, phthalates) and the exposures of different populations (*e.g.*, workers and consumers). However, the OPPT guidance document also notes that the draft methodology may change when it is finalized, based on public comments and ORD's CIA guidelines (note that, as discussed in our comments, the differences between EPA's approaches for CIA and CRA are unclear).
    - ORD's draft CRA guidelines should discuss how its guidelines compare/contrast with the OPPT's guidelines for CRA under TSCA, as well as how each set of guidelines should be considered in risk evaluation and decision-making. A discussion of how the two draft guidance documents will be regarded from a regulatory perspective, including how the

two sets of guidelines might be applied in the context of the fenceline monitoring guidelines OPPT recently proposed under TSCA.

- The recently released proposed approach for a phthalates CRA under TSCA ("Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate Under the Toxic Substances Control Act" [EPA, 2023c]) should be discussed in ORD's draft guidelines for CRA. As generally described in OPPT's proposed principles of CRA under TSCA, the proposed phthalates CRA addresses only chemical exposures and not non-chemical stressors. In addition, only phthalates with a similar mode of action (MoA) would be evaluated through the application of a relative potency factor (RPF) approach (an approach that has historically been applied in risk assessments of several groups of chemicals). Although the RPF approach is not unreasonable for evaluating risk from a subset of phthalates, it is notable that even when TSCA was charged with proposing a CRA, the focus was only on phthalates with an overlapping MoA and did not include an evaluation of other phthalates or non-chemical stressors.
- The proposed phthalates CRA approach includes both phthalate exposures that are TSCA-related and those that are considered "non-attributable" (*e.g.*, household dust) and "non-TSCA exposures" (*e.g.*, diet). In its comments on the proposed approach, the EPA Science Advisory Committee on Chemicals (SACC) expressed concern about the uncertainty in combining TSCA-related phthalate and non-attributable and non-TSCA-related phthalate exposures. It noted that if UFs are used to address this uncertainty, the total UF may be too large, such that the results will be of minimal use (EPA, 2023d). The proposed approach for a phthalates CRA also includes combined individual exposures, such as an individual who may be a worker, a consumer, and a member of the general population (*e.g.*, of a fenceline community).
- ORD should discuss OPPT's proposed approach for a phthalates CRA in its draft CRA guidelines and consider the SACC's comments on the proposal and how they may suggest modification of ORD's draft CRA guidelines. For example, the SACC's comments on how combined UFs may be too large to be meaningful even when the CRA focuses entirely on phthalate exposures (and does not include non-chemical stressors) suggests that there would be similar concerns about the application of UFs that might be considered for non-chemical stressors.
- It is notable that while the discussion of possible methods for addressing non-chemical stressors is lacking in ORD's draft CRA guidelines, so is a discussion or examples of how to conduct a CRA for "releases of multiple pollutants" (EPA, 2023a, p. 3) when the chemicals do not have a similar MoA. This is important for addressing fenceline exposures, which is becoming essential in TSCA assessments and other permitting decisions. As discussed above, not only does OPPT's proposed phthalates CRA not include non-chemical stressors but focuses only on those phthalates with a similar MoA. ORD appears to propose guidelines for CRAs that include multiple chemicals with multiple MoAs and non-chemical stressors.

Therefore, as already discussed, ORD's CRA guidelines need to describe methods and examples that have appropriate tools that can be used to conduct these CRAs. Issuing CRA guidelines seems premature without specific guidance on conducting more holistic CRAs. Also, alignment is necessary for oil and gas enterprises when conducting assessments across

different jurisdictions. There should be some flexibility in approaches but an understanding that assessments should be science based, and applicable across agencies and regulations rather than having different approaches for each agency.

8. ***Integration of Geographic Information System (GIS) Tools:*** EPA and other government entities have dedicated significant resources to developing a geographic information system (GIS)-based screening tools to survey and screen areas for a variety of indicators across environmental, health and sociodemographic indicators. EPA needs to clarify what role, if any, that these tools may play in CRA.

   - The utility of geographic information system (GIS) tools for viewing multiple chemical and non-chemical stressors at once is mentioned in Appendix A of the draft CRA guidelines (in its summary of the 2012-2013 CRA webinars) but not elsewhere. Ready-built repositories of the spatial extent of chemical and non-chemical stressors at various geographic scales, sometimes modeled nationally, are available in numerous EJ-related GIS-based screening tools.
     - **EJScreen:** Includes 13 pollution and sources categories, socioeconomic indicators, health disparities, climate-change-related data, housing information, and critical service gaps, such as lack of health insurance, housing burden, and food deserts.
     - **AirToxScreen:** Includes *total* cancer and non-cancer risks and chemical-specific contribution to total risk for many hazardous air pollutants.
     - **Risk-Screening Environmental Indicators (RSEI) Model:** Includes scores incorporating releases at facilities for up to a decade, with assumptions about chemical toxicity and exposure. These unitless scores can be generated for all facility chemicals and individual pollutants. The density and magnitude of RSEI scores in a community could be used to screen for overall pollution exposure.
     - **Environmental Justice Index (EJI):** A Centers for Disease Control and Prevention tool that provides a national rank of social vulnerability, environmental burden, and health factors.

   While the ecologic data, as used in these tools, are insufficient to test exposure-disease associations, they are potentially helpful for generating hypotheses. Using these centralized data sets in early/screening Tier 0 or Tier 1 assessments could help inform a CRA in the initiation stages. Applying one of these tools in Tier 0 or Tier 1 would suggest that the results from that tool could be used to determine if a more refined analysis is needed. While these tools and other similar tools may inform CRA, it would be advisable for the agency to be clear about where these tools could fit into the CRA process. For example, can data from AirToxScreen be used as part of a Tier 0 or Tier 1 assessment? Further, if the agency discusses EJ-related or GIS-based tools, it will be essential to note that these screening tools are not replacements for a robust CRA.

9. ***The draft CRA guidelines should clarify the distinction between CIA and CRA and define where they overlap or work together.*** A key aspect needing clarification is the distinction between Cumulative Impact Assessment (CIA) and CRA. Providing a clear definition of the boundaries, overlaps, and collaborations between these two approaches would offer greater

clarity to practitioners and stakeholders also considering how each is intended to be used and in what scope or manner.

- As noted by multiple reviewers in the EPA Science Advisory Board's "Consultation on Cumulative Impact Assessments" (EPA, 2022b), it would be beneficial to clarify the distinction between EPA's CIA (EPA, 2022a) and CRA; currently, the definitions are vague and overlap, which results in these terms being used interchangeably. Given the complexity involved in quantifying interactions between non-chemical stressors and responses and the lack of methods and consensus on how to quantify associated risks, EPA should discuss how the two approaches overlap. As defined in the glossary of the draft CRA guidelines, a CRA may be primarily quantitative. Yet, the draft guidelines include a discussion of non-chemical stressors and the use of qualitative approaches. As currently defined by EPA, CIA is potentially a more holistic approach to combining chemical and non-chemical stressors. How would a CRA and a CIA differ in their approaches to evaluating non-chemical stressors? There should be a clear distinction between the two approaches and further justification why both approaches are needed.
- A distinction worth considering is that evaluating non-chemical stressors might best be done using the CIA. EPA is undertaking the complex task of multichemical CRA, such as its recently proposed phthalates CRA (EPA, 2023c). This proposal illustrates that conducting a CRA for one group of related compounds is already a significant effort for the agency. Trying to incorporate less-defined data into a CRA would be challenging to achieve. Given the complex nature of both CIAs and CRAs, it would be helpful to add a case study to the draft CRA guidelines showing a side-by-side comparison of how to address a situation using a CIA *vs*. CRA or how they could work together.

10. Meaningful application of CRAs will require structured guidance with consistent resources for conducting quantitative assessments.

- Quantitative human health risk assessment has been the basis for health-based regulation across EPA programs for decades. A key success factor of human health risk assessment is reliance on a structured process that can be replicated across stakeholders and purposes. The draft CRA guidelines state that the CRA process is not a "'one-size fits all' model" (EPA, 2023a, p. 28). While we recognize that a tailored situation-specific analysis would be needed to address many complex scenarios envisioned under CRA, the open-ended nature of almost every step of the CRA process will lead to risk assessments driven by the risk assessor's preferences. As Section 2.4 of the draft CRA guidelines explains, even the general objective, boundaries, and constraints of a risk assessment are subject to professional judgment. In comparing this to the existing human health risk assessment process, which provides clear direction on selecting chemicals of interest, pathways, and outcomes, it is hard to imagine how any consistent CRA could be achieved. Given a similar problem formulation, there needs to be a road map such that a diverse group of stakeholders could arrive at similar conclusions given the same data.
- The human health risk assessment process has relied on centralized quantitative information used relatively consistently across assessments. For example, IRIS is a centralized source of quantitative chemical dose-response information. Similarly, EPA's

"Exposure Factors Handbook" is a similar consensus source for quantitative exposure information. Having an agreed-upon set of quantitative factors, with a complete understanding of derivation details and associated uncertainties, facilitates a structured and consistent application of quantitative information. This ultimately allows for parity (a critical quality) among assessments and the means to compare relative stressor impacts and risk results. The current CRA draft guidelines need to contain structured guidance on how quantitative or qualitative information should be used within CRAs.

Without an authoritative understanding of the qualitative/ quantitative relationship between a non-chemical exposure and an adverse health outcome, stakeholders will undoubtedly rely on different qualitative/quantitative information to characterize health impacts and potentially arrive at vastly different risk conclusions. This has the potential to complicate the interpretation of meaningful contributors to risk and undermine confidence in individual assessments.

In conclusion, it's important to acknowledge the underlying reality that the scientific landscape needed to achieve the guidance's objectives is still under development. In light of this, we emphasize the critical role of utilizing the best available scientific knowledge to effectively demonstrate the existence or absence of cumulative risks. We look forward to a collaborative effort with the EPA to address the concerns outlined in our comment letter. If you have any further questions or would like more information regarding the information discussed, please contact me at blakeu@api.org or 202.682.8480.

Sincerely,

Uni Blake
Senior Policy Advisor
American Petroleum Institute